

SOLUBILITY ENHANCEMENT TECHNIQUE

INTRODUCTION

Solubility :

The term '*Solubility*' is defined as maximum amount of solute that can be dissolved in a given amount of solvent to form a homogenous system at specified temperature.

The solubility of a drug is represented through various concentration expressions such as parts, percentage, molarity, molality, mole fraction.

USP &BP Solubility criteria

Definition	Parts of solvent required for one part of solute
Very soluble	< 1
Freely soluble	1 - 10
Soluble	10 - 30
Sparingly soluble	30 - 100
Slightly soluble	100 - 1000
Very slightly soluble	1000 - 10,000
Insoluble	> 10,000

IMPORTANCE OF SOLUBILITY

- Therapeutic effectiveness of a drug depends up on the bioavailability and ultimately upon the solubility of drug molecule.
- It is important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response to be shown .
- Any drug to be absorbed must be soluble or present in the form of an aqueous solution at the site of absorption.

Techniques Of Solubility Enhancement

1) Particle Size Reduction

- Conventional methods
- Micronization
- Nanosuspension

2)Hydrotrophy

3)Cosolvency

4)Solubilization by Surfactants

5)Solid Dispersion

- The fusion method
- The solvent evaporation method
- hot melt method

6)pH adjustment

7)High Pressure Homogenization

8) Supercritical fluid recrystallization(SCF)

9) Sonocrystallisation

10) Complexation

11) Spray Drying

12) Inclusion Complex Formation-Based Technique

- Lyophilization/Freeze-Drying Technique
- Microwave Irradiation Method

13) Micro-emulsion

14) Self-Emulsifying Drug Delivery Systems

15) Neutralization

16) Polymeric Alteration

17) Salt formation

1) PARTICLE SIZE REDUCTION

- The solubility of drug is related to drug particle size as a particle becomes smaller, the surface area increases , increase in solubility.
- **TECHNIQUES OF PARTICLE SIZE REDUCTION-**
- **Micronization**
- **Nanosuspension**
- **Micronization:**
- Micronization increases the dissolution rate of drugs through increased surface area; by decreasing particle size, it does not increase equilibrium solubility.
- Micronization of drugs is done by milling techniques using jet mill, rotor stator colloid mil

- **Nanosuspension:**

- This technology is applied to poorly soluble drugs that are insoluble in both water and oils.
- A pharmaceutical nanosuspension is biphasic systems consisting of nano sized drug particles stabilized by surfactants for either oral and topical use or parenteral use.
- The particle size distribution of the solid particles in nanosuspensions is usually less than one micron with an average particle size ranging between 200 and 600 nm.

2) HYDROTROPY:

- Hydrotropy is a solubilization phenomenon whereby addition of large amount of a second solute results in an increase in the aqueous solubility of existing solute.
- Concentrated aqueous hydrotropic solutions of sodium benzoate, sodium salicylate, urea, nicotinamide, sodium citrate, and sodium acetate have been observed to enhance the aqueous

solubilities of many poorly water-soluble drugs.

3) COSOLVENCY:-

● The solubility of poorly soluble drugs in water can be increased by mixing it with some water miscible solvent in which the drug is readily soluble. This process is known as co-solvency and the solvent used in combination are known as cosolvent.

● Co-solvent system works by reducing the interfacial tension between the aqueous solution and hydrophobic solute.

● The cosolvents are having hydrogen acceptor or donor groups with a small hydrocarbon region.

The hydrophobic hydrocarbon region usually interferes with the hydrogen bonding network of water which consequently reduces the intermolecular attraction of water while the hydrophilic hydrogen bonds ensures water solubility.

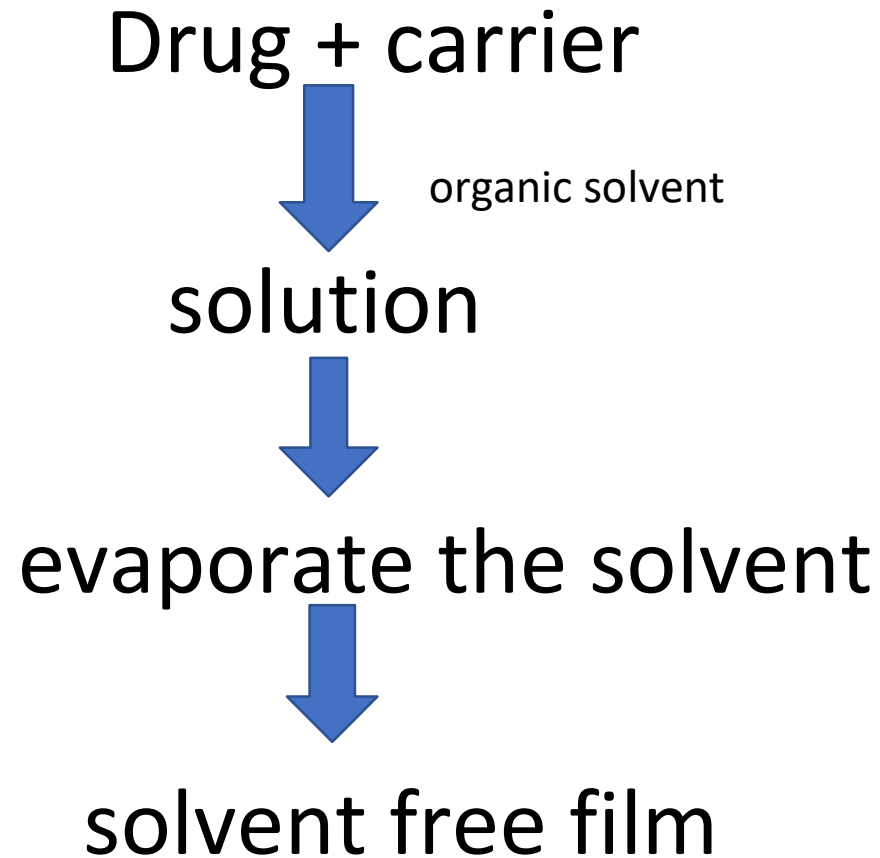
4) SOLID DISPERSION

Solid dispersion is defined as dispersion of one or more active ingredients (hydrophobic) in an inert carrier (hydrophilic) at solid state it is prepared by

- 1) Solvent evaporation method
- 2) hot melt method
- 3) fusion method

Methods of preparation of solid dispersion

1. Solvent evaporation method





dosage forms

In this method the physical mixture of the drug and carrier is dissolved in a common solvent , which is evaporated until a clear , solvent free film is left . The film is further dried to constant weight .

Advantage

- Thermal decomposition of drugs or carriers can be prevented

Disadvantage

- The higher cost of preparation .
- The possible adverse effect of traces of the solvent on the chemical stability

2.Hot melt method

The drug and carrier is typically processed with a twin screw extruder .

The drug and carrier mix is simultaneously melted , homogenized and then shaped as tablet , granules , pellets or powder .

The intermediates can then be further processed into conventional tablets

3.Fusion method

The physical mixture of a drug and a water soluble carrier and heating it directly until it melted. The melted mixture is then solidified rapidly in a ice bath under vigorous stirring . The final solid mass is crushed ,pulverized and sieved .

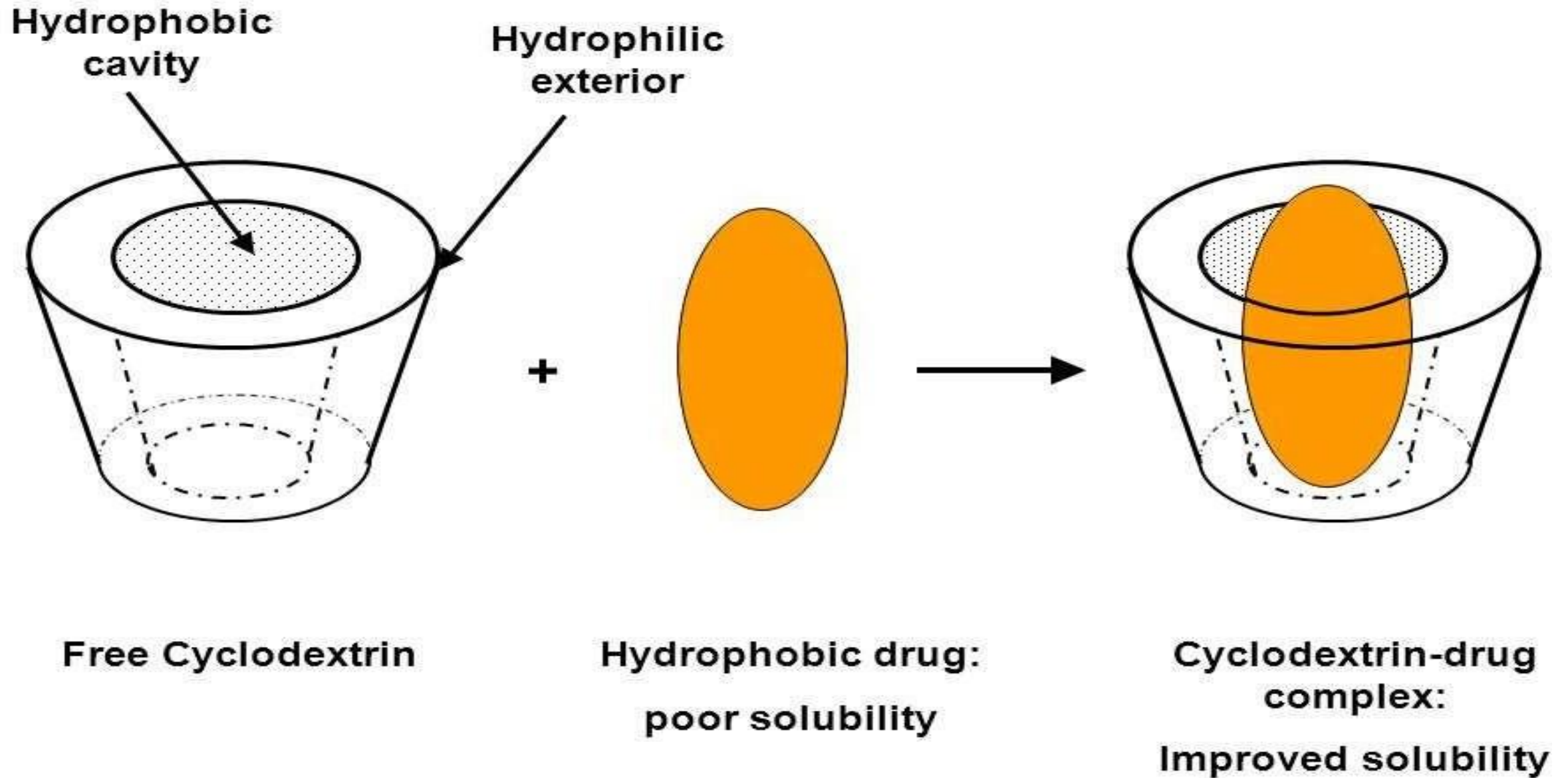
Advantages of solid dispersion

Generally ,solid dispersion is mainly used

- To reduce particle size
- To improve wettability
- To improve porosity of drug
- To decrease the crystalline structure of drug in to amorphous form
- To improve dissolvability in water of poorly water soluble drugs
- To mask the taste of the drug substance .

6)COMPLEXATION:-

- Complexation of drugs with cyclodextrins has been used to enhance aqueous solubility and drug stability.
- Cyclodextrins of pharmaceutical relevance contain 6, 7 or 8 dextrose molecules (α , β , γ -cyclodextrin) bound in a 1,4-configuration to form rings of various diameters.
- The ring has a hydrophilic exterior and lipophilic core in which appropriately sized organic molecules can form non covalent inclusion complexes resulting in increased aqueous solubility and chemical stability.



APPLICATION OF SOLUBILITY

- Solubility is represents a fundamental concept in fields of research such as chemistry , physics, food science, pharmaceutical, and biological sciences.
- The solubility of a substance becomes specially important in the pharmaceutical field because it often represents a major factor that controls the bioavailability of a drug substanc

- Solubility of a substance is useful when separating mixtures.
- Moreover, solubility and solubility-related properties can also provide important information regarding the structure of drug substances, and in their range of possible intermolecular interactions.



THANK YOU